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Newborn Screening in the NICU: Colorado's Experience with Screening Low Birth Weight Infants

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Objectives

- Goals of the project
- Compare the procedures outlined in the 2009 CLSI document NBS03-A “Newborn Screening for Preterm, Low Birth Weight, and Sick Babies: Approved Guidelines” to procedures outlined in Colorado’s Rules and Regulations.
- Methods
- Results
- Conclusions
- Next Steps

Goals

- Perform a baseline evaluation of newborn screening results in the NICU population of Colorado
 - Timing of first specimen collection
 - First NBS obtained before or after blood transfusion
 - Differences in timing of screening in study population as compared to all CO screening and across categories of interest
 - Rate and type of abnormal screening results
 - Regulatory or protocol changes to improve NBS for NICU population
- Conducted as a master's degree capstone project of Genetic Counseling graduate student Jeanine Ashley

Comparison

CLSI 2009 Guidelines

- Screening protocols should be different for newborns requiring intensive care
- Goal: NBS in shortest time, with highest reliability, and fewest specimens
- Recommended 3-step protocol for screening NICU population
- First screen upon admission to NICU, unless already done
- Second screen at 48-72 hours of life if:
 - First screen was before 24 hours
 - Weight was less than 2000g at birth
 - Abnormal results on first screen
- Third screen at 28 days or upon discharge

Colorado Rules and Regulations

- All infants treated the same with exception of transfused infants for collection.
- Specimens are to be collected prior to blood transfusion, if applicable.
- First screening specimen: as late as possible prior to discharge but no later than 48 hours after birth
- Second screening specimen: 8 to 14 days old
- Weight dependent cut-offs for CAH. Follow-up protocols accommodate for TPN.

Methods

- Data query
 - Colorado NBS laboratory demographics and results data extracted from Specimen Gate[®].
 - De-identified
 - Three years: 2012-2014
 - Birth weight, age at first NBS collection, blood transfusion status, screening facility, and results.
- Target population: newborns in CO NICUs
 - Birth weight of 1800g or less used as proxy as NICU status was not collected as a demographic on the NBS card.
 - Compare NICU data to aggregate data of Colorado's population



Methods: data stratification

Birth weight	Category name
400g – 999g	Extremely low birth weight (ELBW)
1000g – 1499g	Very low birth weight (VLBW)
1500g – 1800g	Low birth weight (LBW)

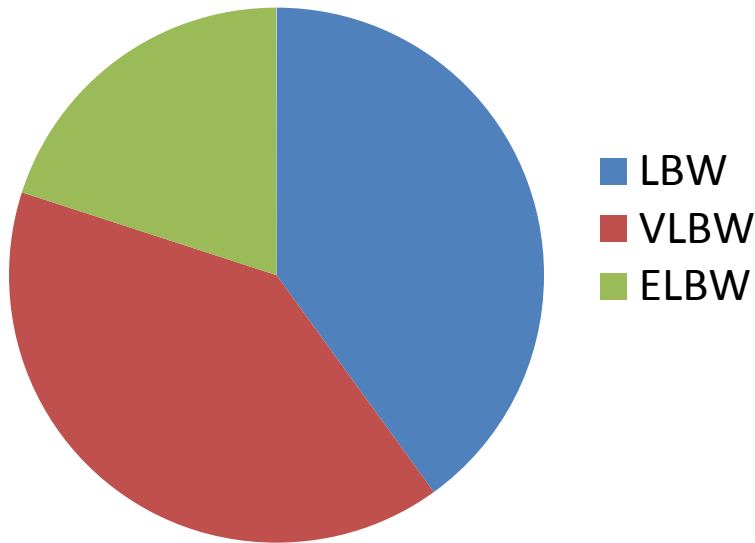
Time of collection	Category name
No entry, -5.05 hrs, 0 hrs	Missing
> 0 to < 24 h	Early
24 h to < 48 h	On time
48 h to < 72 h	Late
72 h to < 300 h	Very late

Facility category	Description	No. of facilities
Level I	Well-baby nursery	10
Level II	Special Care nursery	15
Level III	NICU	16
Level IV	Regional NICU	2

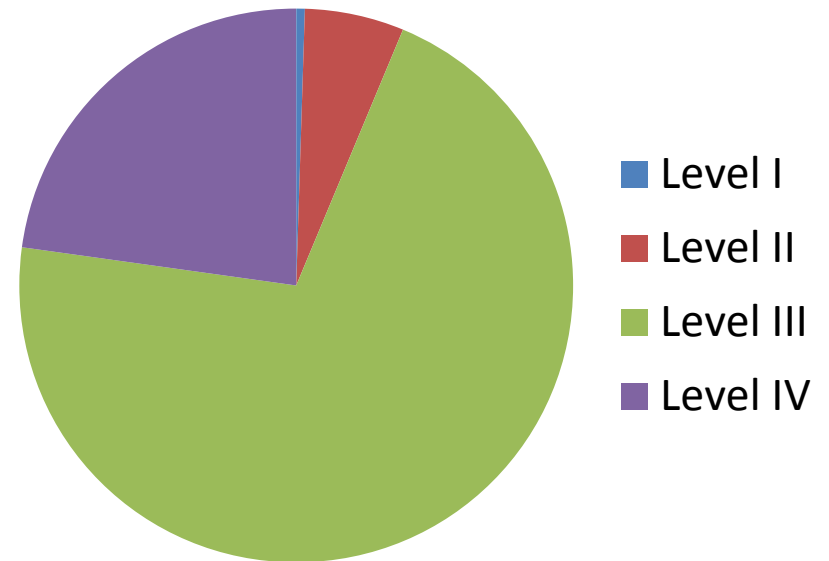
Summary of Data

- 4076 records evenly split over 3 years

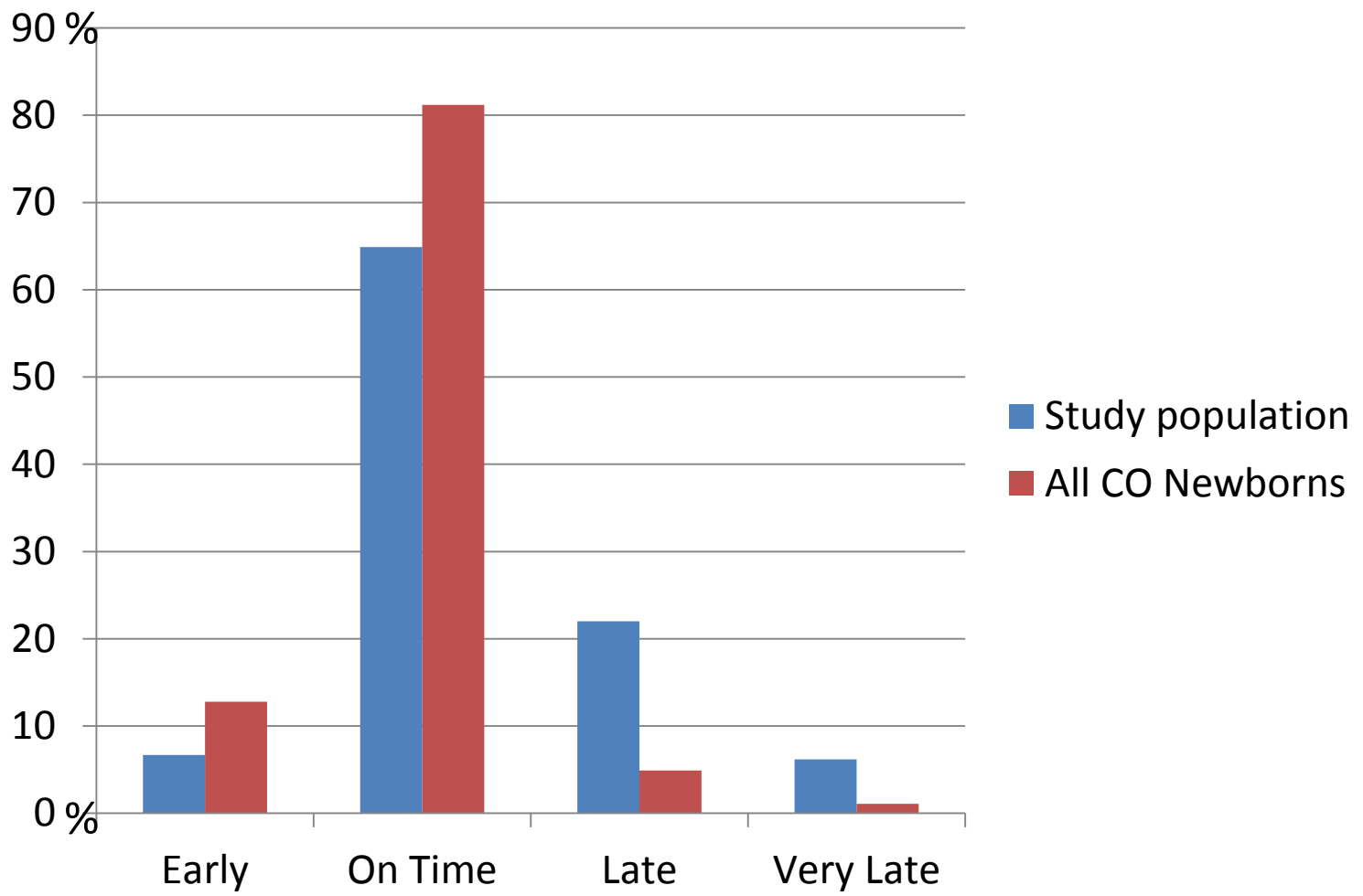
Mean birth weight 1340g



Distribution of screening among Nursery Level



Timing of NBS: NICU vs. All CO Newborns





Blood transfusion status

Transfused prior to screening?	Frequency	Percent
Yes	117	2.9%
No	3700	90.8%
Unknown	259	6.3%



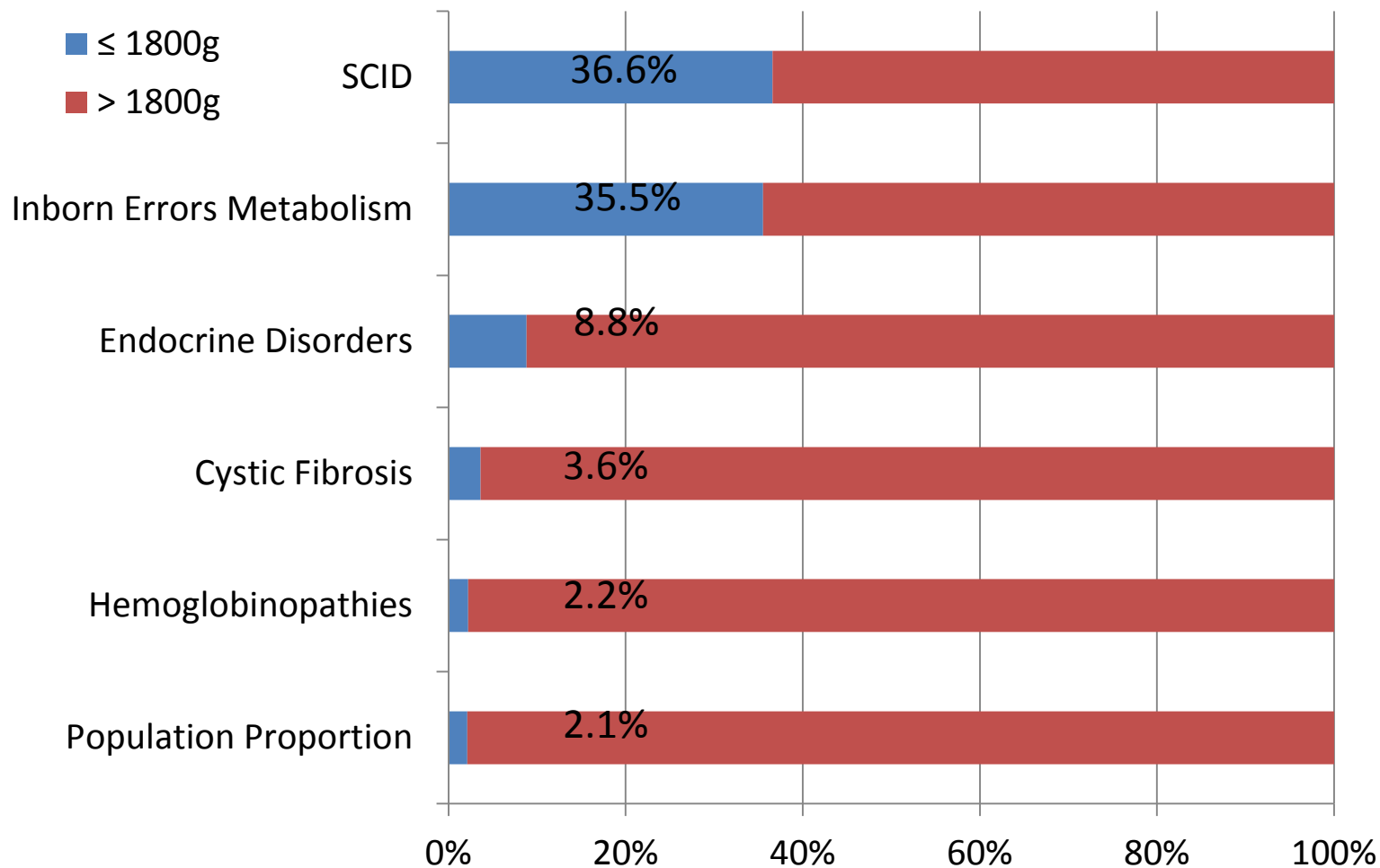
Abnormal Screening Results

- 1372 (not investigated for overlap)
 - Amino acidemias (all 8)
 - Organic acidemias (9 of 11)
 - Fatty acid oxidation disorders (5 of 10)
 - Endocrinopathies
 - Hemoglobinopathies
 - Cystic fibrosis
 - Severe Combined Immunodeficiency)
- True positives? 4
 - Congenital Hypothyroidism

Positive Predictive Values

Disorders		Study population: ≤1800g			Newborns >1800g		
		ABN	TP	PPV	ABN	TP	PPV
Amino Acid Disorders	ARG	223	0	0	232	0	0
	CIT/ASA	2	0	0	6	1	16.7
	HCY/MET	407	0	0	193	0	0
	MSUD	6	0	0	43	0	0
	PKU/HyperPHE	43	0	0	107	26	24.3
	Tyrosinemias	137	0	0	84	0	0
Fatty Acid Oxidation Disorders	CPTI	8	0	0	17	0	0
	CUD	8	0	0	172	2	1.2
	MCADD	9	0	0	57	7	12.3
	SCADD	7	0	0	146	1	0.7
Organic Acid Disorders					110	3	2.7
	C5OH disorders	8	0	0			
	BIOT	6	0	0	165	5	3.0
	GA1	4	0	0	127	2	1.6
	GA2	32	0	0	36	0	0
	IVA	36	0	0	83	0	0
	MAL	2	0	0	45	0	0
PA/MMA	27	0	0	129	2	1.6	
Endocrine Disorders	CAH	86	0	0	604	12	2.0
	CH	44	4	9.1	749	85	11.3
Other Disorders	CF	88	0	0	2384	68	2.9
					7193	26	0.4
	Hemoglobinopathy	163	0	0			
	SCID	26	0	0	45	1	2.2

Abnormal screening results: study population vs. newborns over 1800g





Discussion: Collection Time

- Early screening not worrisome for NICU population as the need to screen before transfusion.
- Late screening (> 48 hours) for 28.8% of the NICU population as compared to 6% of all CO newborns.
 - Risk for screening impacted by treatments
 - Risk for late identification of disorders
 - Risk for false negatives of disorders (FAO disorders)
- Missing information: no time of collection entered for 581 newborns during study period (14.3%)
- *Gap noted: for transferred infants, screening responsibility not defined by CO's rules and regulations.*



Discussion: Blood Transfusion

- 117 infants screened after transfusion
 - Risk of false negatives
- Missing information for 6.3%
 - Don't know the blood transfusion status
- Clinical judgement prevails:
 - Likely to be a small number of infants with screening after transfusion
- *Gap noted: No system in place for following up with the transfused infants nor no guidance provided on reports for risks and need for repeat screening.*



Discussion: Abnormal Results

- NICU population requires a disproportionate amount of NBS follow-up efforts
 - Amino acidemias: TPN
 - Fatty acid oxidation: carnitine, MCT, transfusion
 - Organic acid disorders: antibiotics, hyperbilirubinemia
 - Endocrinopathies: prematurity
 - Cystic fibrosis: prematurity, stress
 - Hemoglobinopathies: transfusion
 - SCID: transfusion, prematurity
- *Gap noted: Minimal information on NBS collection card to assist lab with interpretation of results*
 - Other states include gestational age, type of feeding, antibiotics, hyperbilirubinemia on collection card

Conclusion

- Results illustrated gaps in the Colorado NBS system.
 - Late screening was significantly higher for NICU population
 - No guidance for transfused infants
 - Screening responsibility of transferred infants not defined
- Results demonstrated the burden that NICU populations places on the NBS system.
 - Study population represented disproportionate number of abnormal screening results
 - False positives comprise the vast majority of abnormal screening results for this population

Next Steps

- Revised NBS cards in December 2015
 - NICU status (Y/N)
 - Reason not screened
 - Deceased
 - Transferred (and to what facility)
 - Refused
 - Other
- Updates underway for Specimen Gate[®]
 - Tracking of the new fields with appropriate queries
 - Improved guidance for follow-up of transfused infants

...Next Steps

- Improving NICU educational efforts
 - NICU specific report cards for larger NICU facilities to be created
 - NICU educational presentations scheduled for 2016
- Rules and Regulations changes proposed for 2016
 - Improve language regarding collection
 - Require submission of NBS card for all infants even if not screened
 - Define responsibility for screening of transferred infant

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